

IN THE CLAIMS:

Please cancel claims 1-12.

13. (Amended) An isolated polynucleic acid molecule [sequence] encoding a neurotrophic factor receptor protein comprising an amino acid sequence selected from the group consisting of [as claimed in any one of claims 1 to 8]

- (a) an amino acid sequence of SEQ ID NO:36,
- (b) an amino acid sequence of SEQ ID NO:38,
- (c) an amino acid sequence of SEQ ID NO:40,
- (d) an amino acid sequence of SEQ ID NO:42,
- (e) an amino acid sequence of SEQ ID NO:43, and
- (f) an amino acid sequence of SEQ ID NO:44.

B' 14. (Amended) An isolated polynucleic acid molecule [sequence] encoding a neurotrophic factor receptor protein comprising an amino acid sequence selected from the group consisting of:

- (a) an amino acid sequence comprising Cys⁴⁰ through Cys⁴²¹ of SEQ ID NO:36,
- (b) an amino acid sequence comprising Cys⁴⁴ through Cys³⁸⁹ of SEQ ID NO:38,
- (c) an amino acid sequence comprising Cys³⁶ through Cys⁴¹⁷ of SEQ ID NO:40,
- (d) an amino acid sequence comprising Cys⁴¹ through Cys³³⁷ of SEQ ID NO:42,
- (e) an amino acid sequence comprising Cys⁴⁶ through Cys⁴⁴⁶ of SEQ ID NO:43, and
- (f) an amino acid sequence comprising Cys⁴¹ through Cys⁴³⁵ of SEQ ID NO:44

[as depicted in Figure 2 or 4 (SEQ ID NO: 2 or 4) and analogs thereof wherein the protein is capable of complexing with glial cell line-derived neurotrophic factor (GDNF) and thereby mediating cell response to GDNF].

Please cancel claims 15-16

B² 17. (Amended) An isolated polynucleic acid molecule encoding a neurotrophic factor receptor protein which complexes with a neurotrophic factor, said polynucleic acid molecule

selected from the group consisting of [sequence comprising]:

- (a) a molecule of SEQ ID NO:35 [sequence set forth in Figure 1 (SEQ ID NO: 1)] comprising nucleotides encoding Met¹ through Leu⁴⁶⁴ or SEQ ID NO:37 [Ser⁴⁶⁵ or Figure 3 (SEQ ID NO: 3)] comprising nucleotides encoding Met¹ through Trp⁴⁰⁰ or SEQ ID NO: 39 comprising nucleotides Met¹ through Leu⁴⁶⁰ or SEQ ID NO: 41 comprising nucleotides Met¹ through Trp³⁹⁷ [Ser⁴⁶⁸, wherein said sequence encodes a neurotrophic factor receptor protein (GDNFR) capable of complexing with glial cell line-derived neurotrophic factor (GDNF) and thereby mediating cell response to GDNF];
- (b) a polynucleic acid molecule [sequence] which (1) hybridizes to a complementary sequence of (a) or a degenerate sequence thereof and (2), wherein hybridization conditions are 4 x SSC at 45-55°C or hybridization with 30-40% formamide at 40-45°C, or wherein stringent hybridization conditions are used [encodes an amino acid sequence with GDNFR activity; and
- (c) a nucleic acid sequence which but for the degeneracy of the genetic code would hybridize to a complementary sequence of (a) and (2) encodes an amino acid sequence with GDNFR activity].

18. (Amended) A vector comprising a polynucleic acid molecule of claim 13, 14 or 17 [sequence according to any of claims 14 to 17] operatively linked to one or more operational elements [capable of] effecting the amplification or expression of said polynucleic acid molecule [sequence].

19. (Amended) A vector comprising a polynucleic acid molecule [sequence] encoding a neurotrophic factor receptor protein comprising the amino acid sequence of SEQ ID NOs:36, 38, 40, 42, 43 or 44 [as depicted in Figure 2 or 4 (SEQ ID NO: 2 or 4)] operatively linked to one or more operational elements [capable of] effecting the amplification or expression of said polynucleic acid molecule [sequence].

20. (Amended) A transformed or transfected host cell comprising a [transformed or

transfected with the] vector of claim 18.

B² cont 21. (Amended) A transformed or transfected host cell comprising a [transformed or transfected with the] vector of claim 19.

22. A host cell of claim 20 selected from the group consisting of mammalian cells and bacterial cells.

23. A host cell of claim 22 which is a COS-7 cell or E. coli.

Please cancel claims 24-27

28. (Amended) A method for the production of a neurotrophic factor receptor protein which complexes with a neurotrophic factor protein, said method comprising the steps of:

(a) culturing a host cell, containing a polynucleic acid molecule [sequence] encoding a neurotrophic factor receptor protein comprising an amino acid sequence selected from the group consisting of

- B³
- (i) an amino acid sequence of SEQ ID NO:36,
 - (ii) an amino acid sequence of SEQ ID NO:38,
 - (iii) an amino acid sequence of SEQ ID NO:40,
 - (iv) an amino acid sequence of SEQ ID NO:42,
 - (v) an amino acid sequence of SEQ ID NO:43, and
 - (vi) an amino acid sequence of SEQ ID NO:44

[as depicted in Figure 2 or 4 (SEQ ID NO: 2 or 4) and analogs thereof wherein the protein is capable of complexing with glial cell line-derived neurotrophic factor (GDNF) and thereby mediating cell response to GDNF], under conditions suitable for the expression of said neurotrophic factor receptor protein by said host cell; and

(b) optionally, isolating said neurotrophic factor receptor protein expressed by said host cell.

29. (Amended) A method of claim 28, wherein said polynucleic acid molecule [sequence] encodes a neurotrophic factor receptor protein comprising the amino acid sequence of SEQ ID

NOs:36 or 38 [as depicted in Figure 2 (SEQ ID NO:2)].

30. (Amended) A method of claim 28, wherein said polynucleic acid molecule [sequence] encodes a neurotrophic factor receptor protein comprising the amino acid sequence of SEQ ID NOs:43 or 44 [as depicted in Figure 4 (SEQ ID NO:4)].

B³
cont
31. (Amended) A method for the production of a neurotrophic factor receptor protein comprising the steps of:

- (a) culturing a host cell transformed or transfected with a polynucleic acid molecule [sequence] according to claim 17 under conditions suitable for the expression of said neurotrophic factor receptor protein by said host cell; and
- (b) optionally, isolating said neurotrophic factor receptor protein expressed by said host cell.

Please cancel claims 32-69.

Please add the following claims:

--70. An isolated polynucleic acid molecule encoding a neurotrophic factor receptor protein which complexes with a neurotrophic factor, comprising a molecule which hybridizes to a complementary sequence of a molecule encoding an amino acid sequence of SEQ ID NOs: 36, 38, 40, 42, 43 or 44 under stringent conditions, or under conditions of relaxed stringency wherein said hybridization conditions are 4 x SSC at 45-55°C or hybridization with 30-40% formamide at 40-45°C.

B⁴
71. A vector comprising a polynucleic acid molecule of claim 70 operatively linked to one or more operational elements effecting the amplification or expression of said polynucleic acid molecule.

72. A transformed or transfected host cell containing a vector of claim 71.

73. A method for the production of a neurotrophic factor receptor protein comprising the steps of:

- (a) culturing a host cell, containing a polynucleic acid molecule of claim 70 under conditions suitable for the expression of said neurotrophic factor receptor protein by said host cell; and
- (b) optionally, isolating said neurotrophic factor receptor protein expressed by said host cell.

B4
cont
74. A method for the production of a neurotrophic factor receptor protein comprising the steps of:

- (a) culturing a host cell, containing a polynucleic acid molecule of claim 21 under conditions suitable for the expression of said neurotrophic factor receptor protein by said host cell; and
- (b) optionally, isolating said neurotrophic factor receptor protein expressed by said host cell.--

REMARKS

Claims 18, 20, 22-23 and 26 were objected to as being in improper dependent form. Claim 18 has been amended to refer to other claims in the alternative only, and therefore, the objection may be withdrawn.

Claims 53-58 and 60 have been canceled, and therefore, the objection to those claims may be withdrawn.

The present invention discloses novel soluble polypeptides, that is polypeptides which lack a cytoplasmic or transmembrane domain (see Abstract, page 141, line12). These neurotrophic factor receptor polypeptides or proteins complex with neurotrophic factors such as glial cell line-derived neurotrophic factor (GDNF) or neurturin and thereby mediate cell response to the neurotrophic factor.